from 5 c.c. for infants to 12 or 15 c.c. for older children, when the serum is from a recent convalescent, or ¼ to ½ more when the parent is used. Whole blood serves equally well, but nearly twice as much should be given. A preparation of placental globulin is available which will yield comparable results, though with some tendency to reactions. Otherwise treatment is entirely symptomatic and supportive, except when complications occur.

Complications are most commonly those due to the streptococcus, such as otitis media and adenitis. Pneumonia also is common. These are well treated with chemotherapy.

Encephalitis is an uncommon but serious complication of measles, occurring in about one out of a thousand cases. It may occur at any time from the first symptom until well after apparent recovery, but usually about the time the rash fades. It has no proven treatment, but we have been impressed with apparent benefits of shock therapy. Activation of latent tuberculosis must also be expected.

1635 Chelsea Road.

MENINGOCOCCUS DISEASE*

EDWARD B. SHAW, M. D.
San Francisco

WARTIME and similar conditions have invariably favored the prevalence of meningococcus disease. Present day conditions on the Pacific Coast, abnormal concentration of troups and of civilian workers, crowding and unsatisfactory housing, dubious hygienic conditions, may all be expected to provoke increased incidence of meningococcus disease. In at least some areas of this region increased prevalence may already be noted.

Before the advent of sulfonamides the end results of treatment, with specific antiserum, were dismally poor; but with modern chemotherapy, the infection is readily controlled if treatment is administered early and adequately. The outcome is so dependent on prompt detection and resourceful treatment as to constitute a distinct challenge to medical acuity.

This infection gains entry to the body through the upper air passages where it apparently multiplies and elaborates a specific toxin; thence it is carried through the blood stream to produce varying evidences of sepsis, and finally localizes in a serous surface, usually the meninges.

Primary infection in the nasopharynx is often asymptomatic and almost always escapes etiologic recognition. The succeeding stage of circulatory dissemination is sometimes equally insidious and evidenced only by the eventual localization of the organism. At other times, however, this septicemic stage causes symptoms of varying kind and intensity. In a few instances there is extreme infestation of the blood stream, and the patient rapidly develops signs of profound prostration and shock; there is frequently an accompanying hemorrhagic eruption, and within the course of a few hours meningeal localization occurs if the patient escapes an immediately fatal outcome. There are somewhat rare forms of infection, in which there is prolonged low-grade fever, hemorrhagic phenomena are usually lacking, and the diagnosis is established only by blood culture.

Hemorrhagic skin eruptions do not invariably accompany the septicemic stage, but when they do occur they are so characteristic as to be almost unfailingly diagnostic. In extremely fulminant cases purpuric spots are usually present, inasmuch as they proceed from the underlying cause of the profound symptoms—extensive damage of the vascular bed by the intense toxemia. Early meningitis constitutes a late stage of sepsis during which the existence of petechiae may indicate the nature of the pathogen. The eruption may be sparce or scattered, varying from a few petechiae to extensive areas of cutaneous hemorrhage, and may extend so rapidly that new spots may be observed to appear during the course of examination. Commonly, the lower extremities are more involved than the trunk or upper extremities, and petechiae are frequently found in the conjunctivae or upon the soft palate. Morbilliform, urticarial, or nondescript rashes may accompany the purpuric eruption. Emphasis should not be directed so much to the importance of the eruption as a diagnostic sign, as to the fact that, regarded together with other symptoms, it indicates the meningococcus as the etiologic agent, especially in cases in which delay for bacteriological confirmation may be extremely dangerous.

Meningeal localization produces the classical findings of purulent meningitis. The accession of symptoms is usually fairly abrupt, but may be more gradual and insidious. Fever and prostration are variable; pain in the neck, back and extremities, nausea, vomiting and headache are common symptoms. The patient will be found to have neck and back stiffness, which may be initially mild only to progress to extreme neck retraction and opisthotonos. There is accompanying spasm of the hamstrings, and either diminution or exaggeration of the tendon reflexes.

The intensity of symptomatology may vary considerably, occasionally the disease will be so florid as to make recognition easy, at other times symptoms may be deceptively mild. It is extremely important to note that young infants may proceed through a long course of infection with almost complete absence of characteristic signs, without the presence of bulging of the fontanel, neck-stiffness or retraction, Kernig sign, or high fever, to be clinically recognizable only in late stages of the disease when extensive damage has supervened.

LABORATORY FINDINGS

The diagnosis can frequently be established from clinical signs alone, but it is often necessary, and always desirable, to augment physical examination by appropriate laboratory studies, even if treatment is initiated in advance of this confirmation. The white blood count is usually, but not invariably, elevated in proportion to the fever, the chief increase being in the polymorphonuclear cells. In severe sepsis, the organisms may sometimes be identified in stained blood smears and are often readily detected in smears made from punctured petechiae. Blood cultures and spinal fluid cultures, in meningitis, are usually positive, although the meningococcus is somewhat fragile and growth may be obtained only with careful bacteriology. The spinal fluid may be cultured at the bedside upon ordinary Lodfler's slants (ordinarily employed for throat cultures) with very effective results.

The spinal fluid may be unmodified during the course of severe or even fatal sepsis, but as invasion of the meninges occurs the spinal fluid may successively show first only increased pressure, while, later there may be pleocytosis without the presence of organisms, and finally the fluid becomes purulent, and the organisms are readily identifiable by both stained smears and cultures. In the presence of meningitis the sugar content is diminished in the spinal fluid, this diminution being at once indicative of the nature of the inflammation, and roughly proportionate to the severity of the disease.

DIFFERENTIAL DIAGNOSIS

The septic stages of the disease must be differentiated from other forms of sepsis, in nearly all of which skin

* One of several papers in a symposium on "Communicable Diseases." Papers in the symposium have been collected by Dr. Edward B. Shaw, San Francisco.

manifestations are much less common and do not reproduce the purpuric nature of meningococcemia. Septicemic invasion by staphylococci and streptococci will furthermore usually be more clearly associated with an obvious initial focus of invasion.

Other forms of meningeal invasion are sometimes differentiated from meningococcus infection with difficulty. Most forms of purulent meningitis will usually reveal the causative organism in great profusion in stained smears or in culture, whereas the meningococcus is somewhat more difficult to demonstrate. Other central nervous system infections will occasionally lead to confusion. The various encephalitides usually produce only a slight increase in the spinal fluid cell count. Poliomyelitis produces a clinical picture of neck and back stiffness, hamstring spasm, soreness and tenderness in the extremities, very slight increase in the white blood count, and increase of spinal-fluid cell count to, usually, only two or three hundred, rarely to as much as one thousand. The meningo-encephalitis, which follows mumps, is usually identified by the antecedent infection and is characterized by only a moderate increase of spinal fluid cells to 500 to 1,000, with marked lymphocytic predominance. Similar spinal fluid findings characterize the meningitides of virus etiology, including benign lymphocytic meningitis.

The content of reducing substance in the spinal fluid is of considerable importance in differentiating purulent meningitis from poliomyelitis, encephalitis, and the virus meningitides; in these latter conditions spinal fluid sugar will be normal or slightly increased, and it is almost invariably decreased in all forms of purulent meningitis. The blood sedimentation rate is increased in purulent meningitis, normal in virus infection of the meninges.

The diagnosis is established by a summation of the clinical findings, those indicative of sepsis and those pointing to meningeal inflammation. It is frequently essential to proceed with therapy on clinical evidences alone. In any event, however, adequate bacteriological studies of the blood and spinal fluid should be *initiated* before the institution of specific therapy. This is particularly essential with respect to the exclusion of other forms of purulent meningitis which require much more intense and prolonged chemotherapy than does the meningococcus. One may commence treatment before the laboratory evidence is complete, but if adequate cultures are taken before treatment, bacteriological confirmation can usually be secured within the next 24 hours sufficeint to indicate the sort of treatment thereafter desirable.

TREATMENT

The meningococcus is so extremely sensitive to the sulfonamides that this form of treatment has almost entirely supplanted any other. The infection will usually be controlled by relatively small doses of the sulfonamides. Almost anyone of those commonly employed will be effective: sulfanilamide, sulfapyradine, sulfathiazole and sulfadiazine. The use of sulfathiazole is frequently objected to upon the grounds that the drug does not penetrate the spinal fluid. This objection is not altogether valid, because obviously the desired result is penetration, not of the spinal fluid but of the infected tissues and the clinical results of treatment with sulfathiazole have seemed to be quite effective. The present drug of choice is sulfadiazine, although recent reports indicate that a new member of this series, sulfamerazine, is extremely effective.

The object of chemotherapy is to produce adequate blood stream concentration of the sulfonamide as quickly as possible. The patient should receive a dose of sulfadiazine which, for a small child, is slightly more than one grain per pound, and for an adult is slightly less than one grain per pound, usually not over 120 grains in 24 hours, except for extraordinary indications. The patient who is conscious and coöperative is given the entire daily dose orally within the first two to four hours of treatment. Thereafter, he is given one-sixth of this dose every four hours for two or three days, the dosage being gradually reduced and finally withdrawn in a period of seven to ten days. The patient who is unconscious and uncoöperative is given sodium sulfadiazine as a 5 per cent solution in distilled water, the initial dose being slightly more than one grain per pound for children, and somewhat less than this proportion and not exceeding 75 grains for an adult. Succeeding doses may consist of one-fourth the daily dose as the sodium salt intravenously given every six hours, resorting to oral dosage of one-sixth the daily dose every four hours whenever the patient is sufficiently coöperative. It seems to be advantageous to accompany the drug with sufficient oral dosage of sodium bicarbonate to maintain an alkaline urinary reaction. It is certainly essential that the urinary output be maintained by sufficient intake of fluid to carry out the crystalized drug. Many patients are seriously dehydrated at the height of the disease, and it is essential that before sulfonamides are initially administered, the patient be given sufficient fluid by mouth or by vein to safeguard adequate urinary excretion. For the first 48 hours the sulfadiazine blood level should be ten to fifteen milligrams per cent with a spinal fluid level of about 7.5 milligrams per cent. If these levels are not established, the dosage of the drug should be increased arbitrarily.

This method of treatment is almost astonishingly effective in the great majority of cases, and a successful therapeutic result will usually be attained even when the dosage employed is much less than optimum. Failure of treatment is commonly encountered only when the advance of symptoms is so rapid that the patient dies or is irreparably damaged before adequate levels of sulfonamide are established. The purpose of treatment should accordingly be to establish adequate blood levels quickly enough to arrest the progress of symptoms in advance of an extreme degree of damage. When an effective blood concentration of the drug has been achieved the patient will usually thereafter proceed to satisfactory recovery with a more cautious plan of chemotherapy. It is principally in those patients with fulminant sepsis that the rate of advance of symptoms is so rapid as not to be effectively controlled by chemotherapy alone, and this group of cases accounts for a large percentage of the mortality in any series, in which death occurs during the first 24 hours. These patients should be placed in a special category.

These malignant cases of fulminant sepsis must be promptly recognized as a medical emergency. The patient should be recognized upon clinical evidences and treated without delay for bacteriological confirmation, although blood cultures should be taken at the initiation of therapy for the sake of ultimate confirmation. A continuous venoclysis should immediately be established, and the patient be given 500 c.c. of 5 per cent dextrose in saline. The flow is then interrupted, and the patient given the usual intravenous dose of sodium sulfadiazine in distilled water. The venoclysis of dextrose in saline is again resumed, and into the stream of dextrose solution are introduced 20,000 to 100,000 units of meningococcus antitoxin. The amounts of sulfonamide, dextrose solution and serum are proportioned according to age, severity of infection, and degree of dehydration. Usually the severity of the disease is so great that precautionary testing for horse serum hypersensitiveness may be dispensed with, the existence of extreme degrees of hypersensitiveness is rare, although the serum may be introduced at first in minute amounts which is injected into the tube through which the dextrose solution is flowing and additional

amounts successively injected as the venoclysis proceeds. The use of antitoxin intravenously introduces a slightly increased risk of treatment, and is applicable to only a small percentage of the patients treated, but it is the only method which will effectively reduce the 5 per cent to 10 per cent immediate mortality which occurs in fulminant cases of meningococcemia. The patient may be given intramuscular injections of adrenal-cortical extracts as a supportive measure.

When treatment has thus been instituted, it is thereafter carried on by means of the sulfonamide alone exactly as heretofore described.

SPINAL PUNCTURE

Spinal punctures are performed principally for the diagnosis of purulent meningitis, and many patients will not require additional spinal puncture for any purpose. Unless the hydrostatics of the subdural space are interferred with by repeated puncture, there will usually be no reason thus to relieve pressure, and subsequent punctures need only occasionally to be performed to confirm clinical improvement or recovery, or to determine the adequacy of spinal fluid sulfonamide levels. A majority of patients proceed so rapidly to evident clinical recovery that confirmatory spinal puncture is unnecessary.

PENICILLIN

Penicillin is demonstrably effective against the meningococcus and has been employed to a limited extent in the treatment of this disease. The response to sulfonamide drug is so satisfactory, however, that at a time when supplies of penicillin are limited, the use of this agent in meningococcus infection should be restricted to the occasional patient who is sensitive to the sulfonamides or the extremely rare instances in which the organism is refractory to sulfonamide treatment. Penicillin may be employed in dosage of 10-20,000 units, given intramuscularly every three hours. It is improbable, although apparently not definitely demonstrated, that the introduction of penicillin intrathecally is necessary or desirable as a routine of treatment of meningococcus disease. Unquestionably penicillin, in common with almost every other agent which may be introduced intraspinally, produces meningeal irritation and spinal fluid pleocytosis, which is confusing to the clinician and is therapeutically disadvantageous.

There is little doubt that at the present time the sulfonamide drugs are an almost completely adequate agent for the control of meningococcus disease.

PROPHYLAXIS

The communicability of endemic meningococcus disease is extremely low and contact cases are the exception. When there has been intimate contact within a family it is sometimes appropriate to safeguard contacts by the administration of sulfadiazine in doses of about one-half grain per pound per 24 hours for two or three days, which acts as an effective prophylactic. In the epidemic form of the disease in which bacteriological studies have revealed a high carrier rate in army camps or barracks, the use of similar dosage of sulfadiazine for 48 to 72 hours in the entire personnel will reduce the number and viability of organisms which are harbored, and this has been shown to be an effective measure in the arrest of epidemics.

384 Post Street.

No education, no refinements of civilization can compensate a people for the loss of their hardy virtues. The greatest danger of a luxurious civilization is that it is likely to lead a people to lose their fighting edge.—Theodore Roosevelt.

ACUTE ANTERIOR POLIOMYELITIS*

HENRY BRAINERD, M. D.
San Francisco

MUCH attention has been focused on the problems of poliomyelitis by the controversy aroused following the introduction of the Kenny concept,[1] and, more recently, by the epidemic prevalence of the disease.

The etiological agent is a filterable virus which has been isolated from the nasopharyngeal secretions[2] and stools[3] of affected patients, as well as from the excreta of apparently healthy individuals. The virus may occur in sewage,[4] probably in contaminated milk, food and water, and may be passively carried by the housefly.[5]

The concept of entry through the olfactory end-plates has largely been discarded. Portals of entry may presumably be either through the gastroenteric tract[6] or the nasopharyngeal mucosa,[7] whence the virus is transmitted along autonomic nerve trunks to the central nervous system.

Dissemination of the virus within the central nervous system is widespread, but certain sites of predilection are most prominently involved. Many cells are damaged temporarily by the virus and later recover, but some are permanently destroyed in a spotty fashion. In those cases exhibiting flaccid paralysis, anterior horn cell destruction is marked. In numerous cases in which muscle spasm predominates lesions of the small internuncial neurones of the anterior horn have recently been described.[8]

CLINICAL OBSERVATIONS

In the light of recent observations, both the Kenny concept and the older orthodox concept appear to suffer from over-simplification. The relationship of the pathological physiology of the disease to the clinical picture is now in a state of revision.

Following exposure of a group of individuals to poliomyelitis several alternative courses may ensue. In most cases no infection will occur due to the presence of neutralizing antibodies. A smaller group of exposed individuals, after an incubation period of, most commonly, a week, but varying from four to eighteen days, will develop a systemic disease of no specific diagnostic features. Moderate fever, accompanied by nausea and vomiting, diarrhea or constipation, abdominal pain, or symptoms of infection of the upper respiratory tract, may occur. These symptoms, persisting for a few days, may constitute the entire illness, and the diagnosis may be only suspected clinically, unless the virus be isolated or a rise in neutralizing antibodies be demonstrated.

In a still smaller group of exposed persons the disease may progress to a point where it becomes clinically recognizable as involving the central nervous system. Evidences of nervous involvement may develop during the course of the prodromal illness described above, or may succeed it after an asymptomatic interval of several days. Rarely paralysis may occur abruptly without a disease of onset.

In a majority of persons in whom nervous system invasion is manifest, muscle spasm dominates the picture.[9] Although the pathogenesis of this phenomenon is the subject of debate,[8,10,11,12] clinically it is quite striking, and may of itself be the cause of persistent disability. Spasm consists of hyperreactivity of muscles to stretch stimulation, and is manifested by limitation of motion of

---

* One of several papers in a symposium on "Communicable Diseases." Papers in the symposium have been collected by Dr. Edward B. Shaw, San Francisco.

From the Divisions of Medicine and Pediatrics, University of California Medical School; Department of Pediatrics, Stanford University Medical School; and Department of Public Health, City and County of San Francisco.